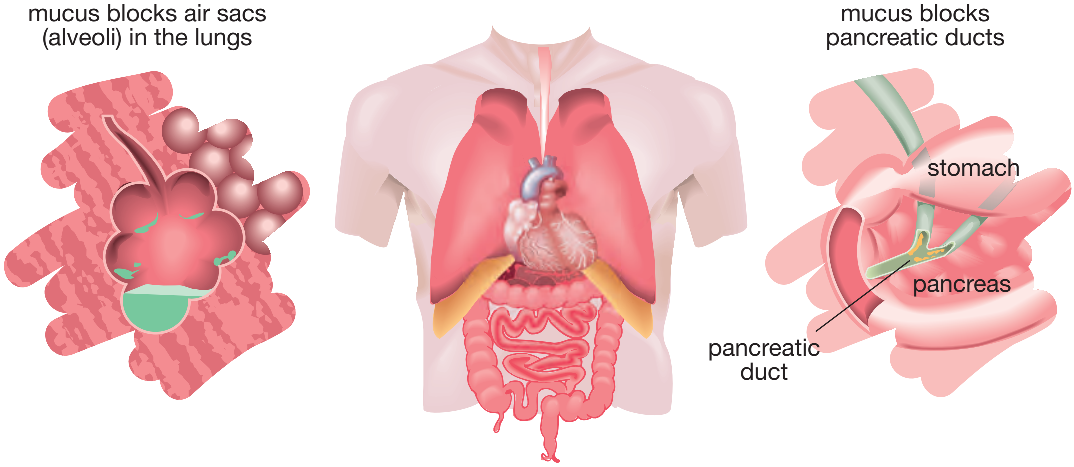
2.4 *Mutations and Genetic Diseases*

Rain or shine, people will show their support for a fundraising walkathon. The Great Strides Walk is held annually to support the efforts of the Cystic Fibrosis Foundation. In 2006 this event raised more than $775 000, as thousands of Canadians participated in more than 40 locations.

The Effects of Cystic Fibrosis



Cystic fibrosis is an inherited condition. It affects the cells that produce the juices of mucus, sweat, saliva, and digestion. One of the functions of these secretions is to act as lubricants, so they normally have thin and slippery consistencies. In cystic fibrosis, a defective gene causes these secretions to become thick and sticky. The result is that they can plug up lung and pancreas passageways.

Earlier in Chapter 2 you learned that genes are like recipes or sets of instructions. You also learned that the sequence of bases in the DNA molecule is comparable to the letters in the words of a written recipe. Imagine that you are copying down a set of instructions in a recipe and you don't notice that you made a mistake. How could the mistake affect your finished product? What if a mistake is made during DNA replication and the base sequence of DNA is copied incorrectly? What effect might such a change have in the DNA sequence, its structure, or how it affects the protein product derived from this DNA molecule?

A change in the sequence of bases along DNA is called a **mutation**. When you hear the word *mutation*, you might think of a science fiction story or a horror movie where a dramatic event causes a character to become described as a mutant with a changed appearance or abilities. Most mutations are actually small changes to the DNA sequence that occur naturally, or are due to exposure to high energy radiation or chemicals. An important characteristic of mutations is that the changes to DNA are carried forward in subsequent DNA replications and are inherited by future generations.

mutation: a heritable change in the sequence of nitrogen bases along a DNA molecule

Figure A2.15: Mutations are responsible for variations within a species.

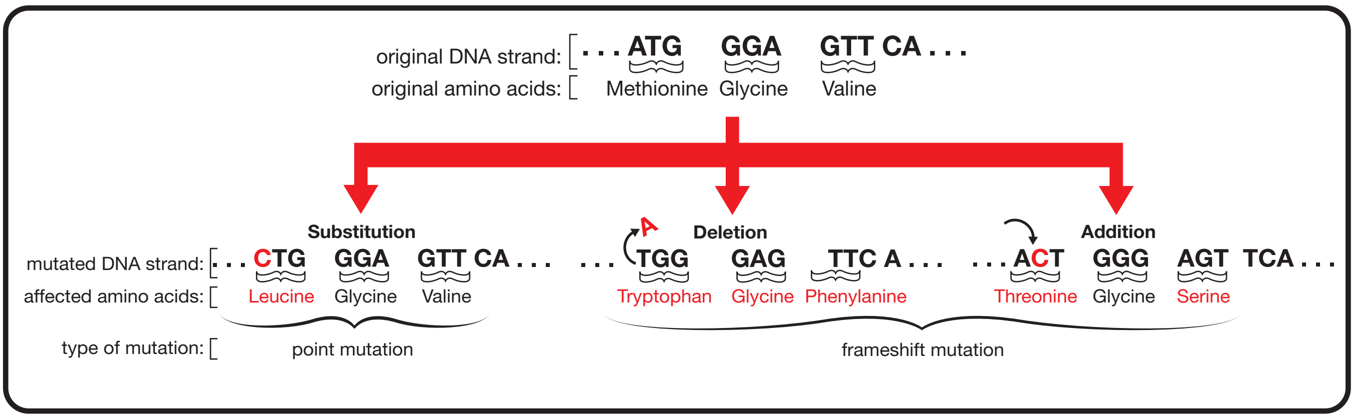
As you learned in previous science courses, mutations are the source of variation within wildlife populations. This variation leads to adaptations, which are acted upon by natural selection to drive evolutionary change. Mutations clearly play an enormous role in the study of biological systems.

In this lesson you will learn how mutations in DNA affect the proteins produced. This occasionally results in human diseases that can be inherited by offspring. Using Mendel's theories and Punnett squares, you will predict the probability of offspring inheriting a genetic disease. You will also learn how to read a pedigree chart that traces genetic diseases through families. Mutations that benefit an organism and mutations that result in resistance to bacteria will also be examined in this lesson.

Mechanisms of Mutation

Mutations are like "typos" in a word-processing document. For both recipes and genes, the effect that a copying mistake has on the product depends on where it happened and on what kind of mistake was made. For example, if you made a slight spelling mistake to the word *salt* and instead wrote *saltt* when copying a recipe, it wouldn't change how you carry out the recipe. And it would have little effect on the finished product. The recipe would still work. But if you wrote *25 mL of salt* instead of the original *2.5 mL of salt*, your recipe would most likely be ruined. In most cases, the mutation of DNA has little effect on the products produced from a gene—the mutations occur in chromosome regions that do not include genetic instructions, or the affected gene sequence is still able to function despite the mistake. Cells can usually repair minor DNA mutations that frequently occur in the human body. Mutations to DNA can occasionally cause the gene to stop working or to work differently, as is the case with cystic fibrosis.

How Mutations Affect Genetic Information



Mutations in DNA can happen when one nucleotide—during replication—accidentally gets substituted for another nucleotide. The chart "How Mutations Affect Genetic Information" illustrates what happens when there is a substitution of one nucleotide—ATGGGAGTT changes to become CTGGGAGTT. The amino acid chain produced from this sequence is now altered, possibly affecting the protein functioning. A nucleotide base substitution is called a **point mutation**, which is similar to a typo where one letter of a word gets changed and often alters the word's meaning. If the phrase "the fox can run" was mistyped as "the box can run," the single letter substitution not only changes the meaning of the phrase but it makes the phrase confusing.

The deletion or addition of a nucleotide can also affect the DNA base sequence resulting in an altered or incomplete amino acid chain. The results tend to be more serious in this case because all of the nucleotides "downstream" of the mutation are affected. In other words, the grouping into sets of three or the framing of all the nucleotides that follow is changed. That is why this is called a **frameshift mutation**. If the phrase "the fox can run" had an extra letter added at the beginning of the phrase but the phrase was still separated into three-letter words, it would read "ath efo xca nru n." The frameshift mutation turns the original phrase into nonsense.

point mutation: the substitution of one nucleotide base for another during DNA replication

frameshift mutation: the deletion or addition of a nucleotide during DNA replication

This change causes the three-letter groupings or frames in DNA to be read in an alternate pattern.

Practice

35. Figure A2.16 shows two DNA strands—the lower strand is a product of replication. A mutation occurs in the middle of a gene sequence. The sequence of bases gets changed from TAT to TAA.

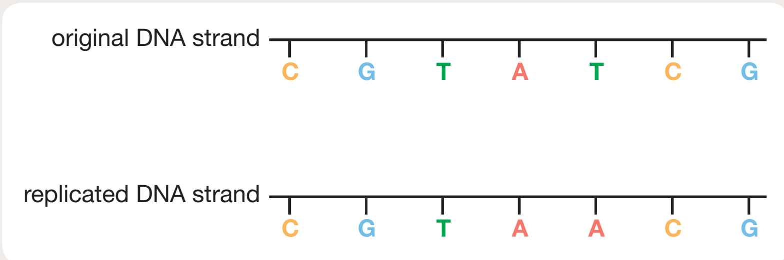


Figure A2.16

- **a.** Is this a point mutation or a frameshift mutation?
- **b.** Use your table "DNA Triplet Codes and Their Corresponding Amino Acids" to identify what amino acid corresponds with the DNA sequence of TAT.
- **c.** What corresponds with the DNA sequence of TAA?
- **d.** Explain what effect the change to the DNA sequence has on the production of the amino acid chain.

36. A gene sequence reads GGATTAGAG. A mutation occurs and the sequence now appears as GGGATTAGAG.

- **a.** Identify the sequence change as either a point mutation or a frameshift mutation.
- **b.** Use your table of DNA triplet codes to list the amino acid sequence produced by the original DNA strand.
- **c.** Use your table of DNA triplet codes to list the amino acid sequence produced by the new, mutated strand.
- **d.** Explain the effect of this sequence change on the production of the amino acid chain.

Passing On Mutations

When you think of a disease you probably think of an illness spread by a disease-causing pathogen, but some illnesses result from the presence of one or several mutated genes. Initially, a mutation can be caused in one individual by an exposure to something in the environment, such as X-rays, ultraviolet radiation, toxic chemicals, or some other factor that causes a change to the nitrogen bases in DNA. The mutations that result often have little effect on the functioning of our bodies. However, in other instances the mutation impairs the function of a gene or the amino acid chain produced, which results in negative consequences for the individual.

If a mutated gene is present in one body cell and that cell is no longer able to fulfill its role, the cell usually dies and other body cells of the same type compensate for the loss of one faulty cell. Recall that there are not only body (somatic) cells but sex cells, such as eggs and sperm. What effect could a mutation have in the genes of a sex cell?

If a mutation is capable of being passed between generations and if that mutation results in illness, then the resulting condition is called a **genetic disease**. Cystic fibrosis is a genetic disease passed on from parents to their children. In this case, chromosome 7 carries the mutated gene that results in the disease.

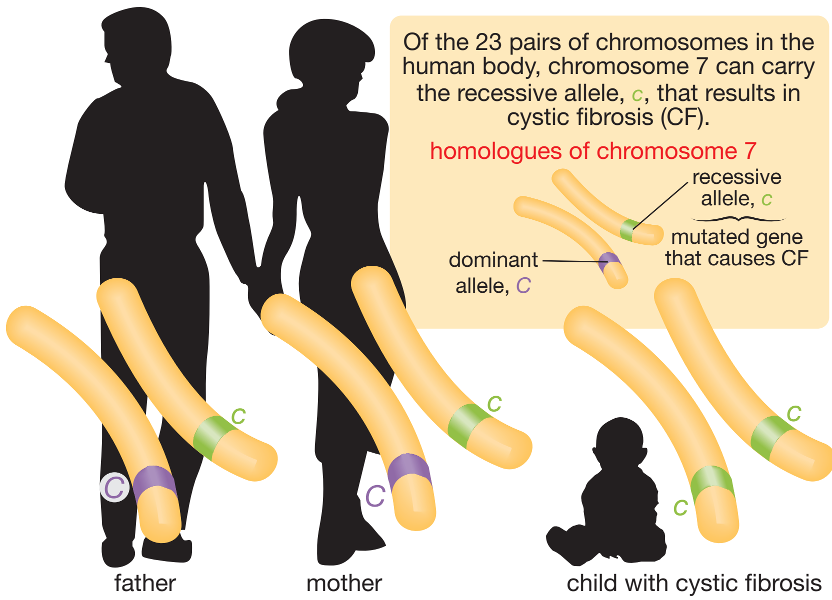
When the gamete with the mutation combines with the gamete of the other parent to produce offspring, the mutated gene is present in every cell of the newly developing offspring. The presence of this mutated gene in each cell can cause the offspring to develop abnormally, die at an early age, or develop a genetic disease. Recent advances in medications and therapies can allow an individual to live longer with an improved quality of life. In spite of this, genetic diseases like cystic fibrosis are difficult to treat and cure because the illness is caused by a mistake in the genes of every body cell, rather than a foreign invading pathogen.

Having one set of genes from each parent can result in a decreased incidence of genetic disease. In many genetic diseases, symptoms are associated with a mutation. The inheritance of a non-mutated copy of a gene from one parent can often compensate for the mutations present in the gene inherited from the other parent. This is why some individuals carry a mutated gene but do not develop the symptoms of a genetic disease. The non-mutated copy of the gene that they received from their other parent is working properly to produce the necessary protein to keep them healthy. An individual who possesses a disease-causing, mutated copy of a gene but who does not develop the symptoms of that genetic disease is called a **carrier**. When a carrier of a genetic disease has a child, there is an increased chance of the child developing the genetic disease. When doctors and other medical practitioners ask about your family history of certain diseases, they are trying to determine the probability of you developing genetically inherited diseases or conditions.

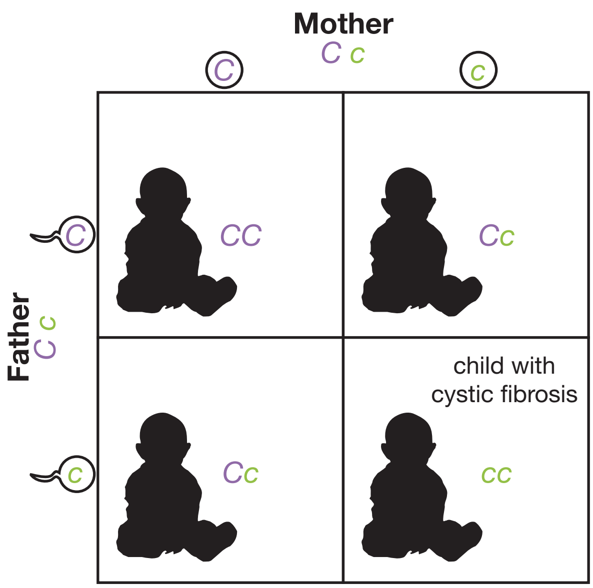
genetic disease: a disease caused by a mutation of one or more genes that can be inherited by future generations

carrier: an individual who possesses a form of a gene (allele) that results in a disease but does not demonstrate, exhibit, show, or have the symptoms of that disease

However, this individual can pass the disease-causing allele to his or her offspring.



Each parent carries the dominant allele, C, and the recessive allelle, c. A Punnett square can be used to show that the probability of their offspring inheriting two recessive alleles is ¼ or 25%.



Note that both parents and probably half of the children will be carriers of cystic fibrosis because they have the genotype Cc.

Practice

37. In your health file, indicate any genetic diseases that run in your family. Some examples of genetic diseases include the following: Tay-Sachs disease, sickle cell anemia, phenylketonuria (PKU), Huntington disease, hemophilia, cystic fibrosis (CF), albinism, Marfan syndrome, polycystic kidney disease, Zellweger syndrome, Adrenoleukodystrophy (ALD), achondroplasia, and maple syrup urine disease.

If you are not sure whether a medical condition in your family is a genetic disease, you can try entering the phrase, "Is ____________ a genetic disease?" in your Internet search engine.

Patterns of Genetic Disease Inheritance

Genetic diseases can be caused by alleles that behave similarly to other recessive or dominant alleles, and they can be autosomal or sex-linked in their mechanisms of inheritance. If the genetic disease is caused by a recessive allele, what genotype would a person with the genetic disease possess? A dominant allele?

If the disease is caused by a recessive allele, an individual requires two copies of a mutated recessive allele (homozygous recessive) to develop the disease. If caused by a dominant allele, only one copy of the mutated allele (heterozygous dominant or homozygous dominant) is needed to cause the disease to develop. Check the following table.

TABLE OF GENETIC DISEASES

Genetic Disease	Symptoms	Location of Gene	Mechanism of Inheritance	Prevalence
cystic fibrosis (CF)	People with CF produce thick sticky mucus that builds up in their lungs and digestive tract. This makes it difficult to properly breathe and digest food. People with CF are also prone to lung infections because they cannot easily clear bacteria from their lungs.	chromosome 7	autosomal recessive	Approximately 1 in 2500 children born in Canada has CF and 1 in 25 Canadians is a carrier of the defective allele that causes cystic fibrosis.
Huntington disease (once called Huntington's chorea)	Huntington disease causes brain cells to die in particular regions. This results in a continual reduction in the ability to control movements, remember events, make decisions, and control emotions. Symptoms usually appear between the ages of 30 and 45.	chromosome 4	autosomal dominant	Approximately 1 in 10 000 Canadians has Huntington disease.
hemophilia	There are two forms of this disease: hemophilia A and hemophilia B. Both forms are caused by a mutation of one of the genes that produces blood-clotting proteins. Both of the genes involved with producing the proteins for blood clotting are found on the *X* chromosome. A defective allele for either of these two *X*-chromosome genes can result in impaired blood-clotting ability. People with hemophilia bleed for a longer time period than people without this condition. Internal bleeding, or hemorrhaging, is a common risk associated with this dangerous condition.	*X* chromosome	sex-linked recessive	Hemophilia A affects about 1 in 10 000 people in Canada and hemophilia B affects as few as 1 in 50 000 people. Because of the sex-linked nature of the disease, males develop the disease more than females do.

Practice

Use the following information to answer questions 38 to 40. When genetic diseases are controlled by a single pair of alleles, the patterns of inheritance described by Mendel's studies and depicted using Punnett squares can help determine the probability of offspring developing a genetic disease. For each of the following crosses involving the inheritance of genetic diseases, choose letters to represent alleles, draw a Punnett square for each cross, and answer the questions about the cross.

38. A couple discover that they both have a family history of cystic fibrosis. They are thinking of having a child, and they ask for a genetic test to be done. Both the man and the woman discover that they are carriers of the recessive cystic fibrosis allele.

- **a.** Build a Punnett square to describe this cross.
- **b.** What is the percentage probability that their child will develop cystic fibrosis?
- **c.** What is the percentage probability that their child will be a carrier of the cystic fibrosis allele?
- **d.** What is the percentage probability that their child will not inherit the cystic fibrosis allele?

39. A man is heterozygous for the dominant Huntington allele, and he has a child with a woman who does not have a Huntington allele.

- **a.** Build a Punnett square to describe this cross.
- **b.** Write the possible offspring genotypes from this cross.
- **c.** What is the percentage probability that their child will not develop Huntington disease?
- **d.** What is the percentage probability that their child will develop Huntington disease?

40. A woman carries one of the defective recessive alleles on her *X* chromosome that causes hemophilia. She has a child with a man who does not possess the hemophilia allele.

- **a.** Build a Punnett square to describe this cross.
- **b.** What is the percentage probability that she will have a child with hemophilia?
- **c.** What percentage of females born from this cross are likely to have hemophilia?
- **d.** What percentage of males born from this cross are likely to have hemophilia?

41. Use the Internet to gather information about the specific organizations in Canada that raise funds and provide support for persons with the following genetic diseases.

- **a.** cystic fibrosis
- **b.** Huntington disease
- **c.** hemophilia

In each case, find the organization's website. Use the site to determine the organization's mission statement and opportunities for people to volunteer or make donations.

Factors That Increase Mutations

Environmental influences can affect the frequency with which mutations occur naturally. People are exposed to some chemicals and electromagnetic radiation that have been shown to increase the frequency of mutations that occur in the human body. An environmental influence that increases the chance of mutation is called a **mutagen**. A mutation in body cells may cause a mistake in the genes that control cell division, resulting in the uncontrolled division of body cells. The abnormal and uncontrolled division of body cells is called *cancer*, and a mutagen known to cause cancer is called a **carcinogen**. Common carcinogens include many chemical agents found in ionizing electromagnetic radiation—such as ultraviolet rays and X-rays —as well as agents in cigarette smoke and pesticides.

mutagen: any agent that causes the likelihood of mutations to increase

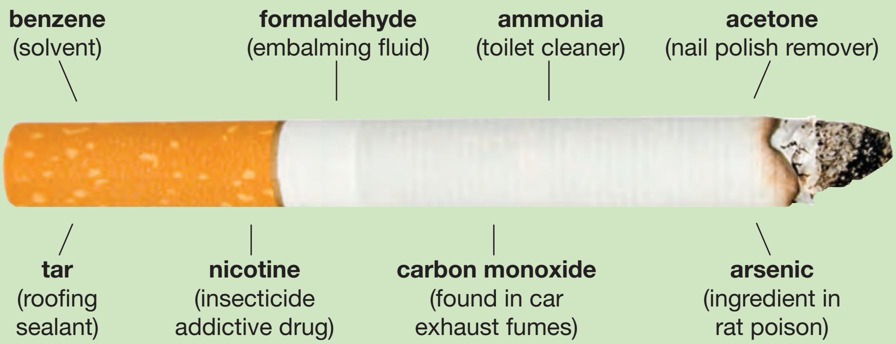
carcinogen: any agent that causes the likelihood of cancer to increase

Many carcinogens are also mutagens.

Science Links

What's the definition of a cigarette? One official in the health-care field described a cigarette as ". . . a delivery system for toxic chemicals and carcinogens."

There are more than 4000 chemicals found in cigarette smoke. And 40 or more of them are known carcinogens, including benzene—a petroleum solvent—and formaldehyde, which is used to preserve dead bodies. In Unit B you'll learn more about the chemistry of some of these toxic organic compounds.



Tracing Genetic Disease: Pedigree Charts

If you observe an individual with a dominant trait, such as the ability to roll her tongue, can you tell if that individual is homozygous or heterozygous for the dominant allele? Is it possible to tell if this person carries a recessive allele? Is there a simple way to detect whether his or her genotype is *Rr* or *RR*? Unfortunately, there is no way to do so by only looking at this specific person, but if you can look at the individual's family, sometimes the answer is staring directly at you. For example, if two tongue-rolling individuals have a child without tongue-rolling ability, it indicates that they both carry the recessive gene for tongue rolling. They would both have to be heterozygous ($Rr \times Rr$) to produce a child who is homozygous recessive (*rr*).

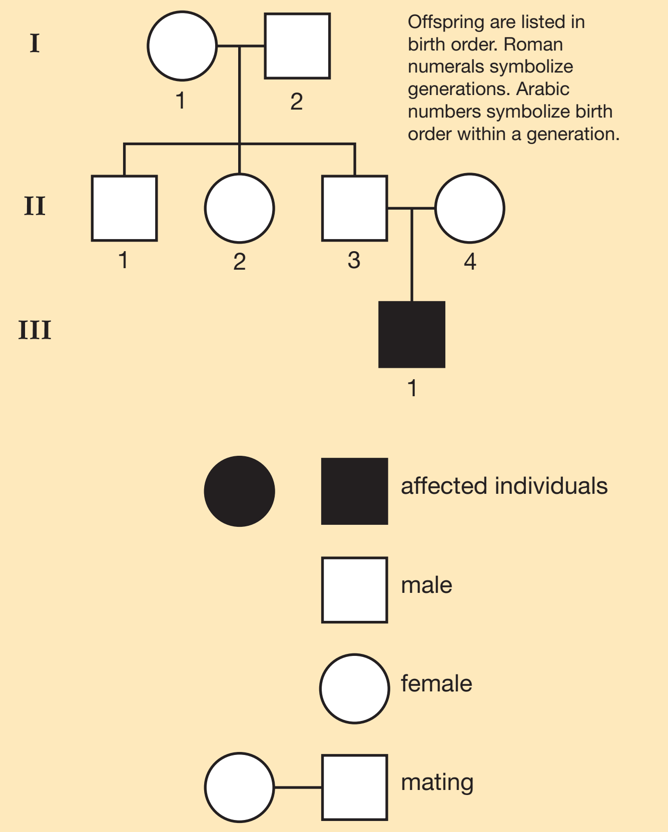
Geneticists use a tool called a **pedigree** to predict the genotype of an individual. A pedigree is like a genetic family tree. You may have previously heard the term in relation to dog breeding or horse breeding. This is because many animal breeders keep detailed lineage records of the animals they breed, and then they use the pedigrees to trace specific traits. A pedigree is a useful technology for tracing genetic diseases.

Genetic pedigrees use a specific set of symbols to identify known genotypes of family members so that unknown genotypes can be predicted. Circles are used to represent females, and squares are used to represent males. On some pedigree charts, a shaded individual indicates a person with the condition being studied. Individuals who are known carriers are sometimes identified by being drawn as half-shaded. A line drawn between two individuals indicates that they have had offspring. Roman numerals and a new row are used to indicate each generation, and individuals are numbered within each generation.

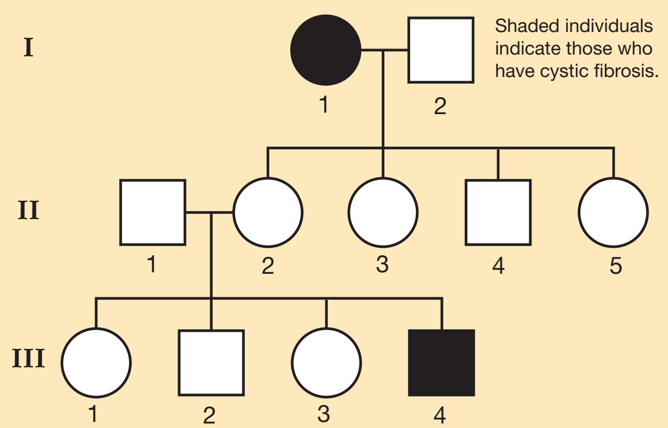
The "Cystic Fibrosis Pedigree" is for a family with members who have the autosomal recessive genetic disease known as cystic fibrosis.

The "Cystic Fibrosis Pedigree" reveals that a first-generation couple had four children—three girls and one boy. The shading indicates that the first generation female (I-1), or the grandmother, had cystic fibrosis. This means that she had to possess two recessive alleles for the condition. The pedigree also shows that none of her four children developed the disease, since the symbols to represent them are not shaded. Because the mother only has the recessive allele to donate, her children all received the allele for cystic fibrosis. Each of her children is a carrier for the disease. Her eldest daughter (II-2) had four children, and the youngest son (III-4) of this daughter developed the disease. In order for this grandson to have the disease, his father (II-1) also has to be a carrier of the recessive allele.

A Guide to Pedigree Charts



Cystic Fibrosis Pedigree
(Autosomal Recessive)



pedigree: a set of standard symbols used as a tool for geneticists to trace a particular trait

It is like a genetic family tree.

The pedigree in Figure A2.17 is for a family with members having the autosomal dominant genetic disease called Huntington disease. A trait that re-appears in each successive generation, as with Huntington disease, is usually caused by a dominant allele.

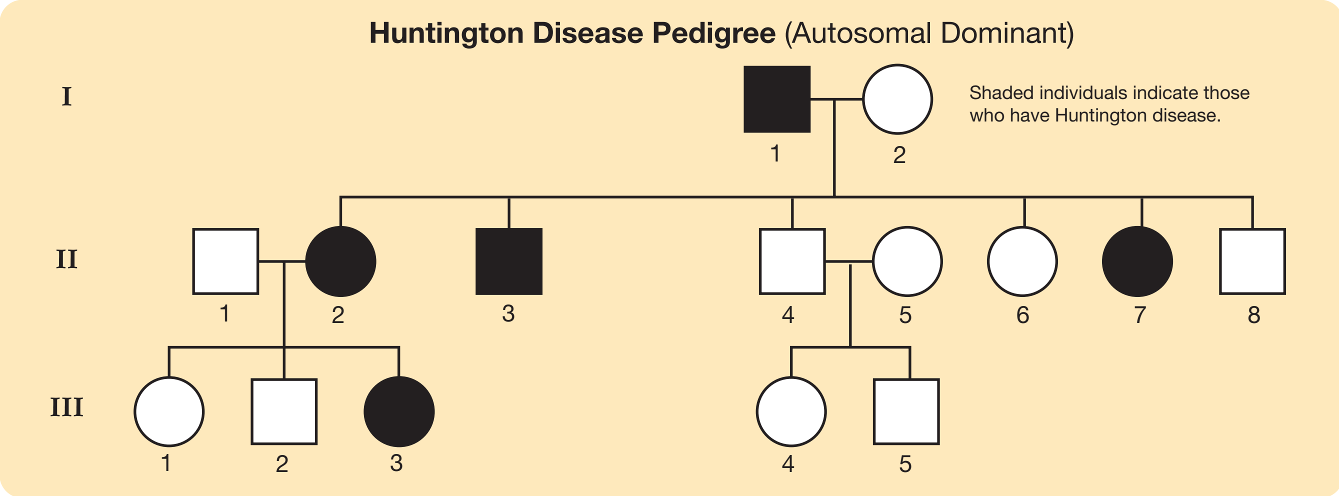
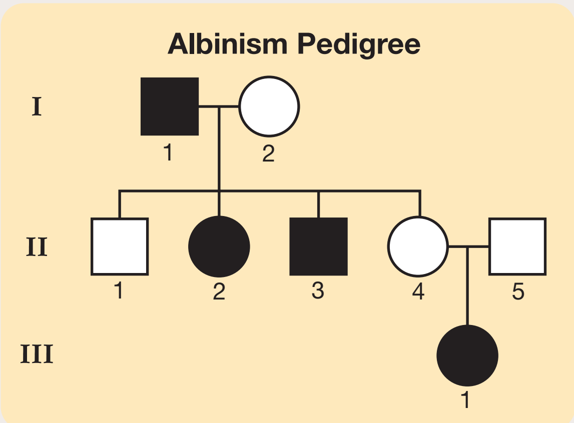


Figure A2.17

Practice

42. Albinism is a genetic condition that causes an absense of pigmentation in skin, hair, and eyes. In humans, the most severe form of albinism—called *oculocutaneous albinism*—is an autosomal recessive genetic disease. Examine the "Albinism Pedigree" and answer questions 42.a. to 42.c.



a. In the pedigree shown, determine the number of females with the albino condition. Determine the number of males with the albino condition.

b. Describe the phenotype of the individual (III-1) and her parents. Account for the differences between phenotypes in these two generations.

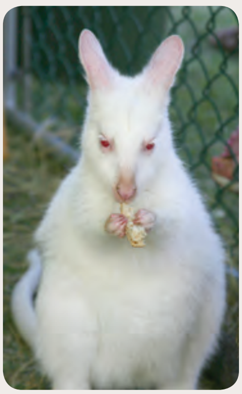


Figure A2.18: albino wallaby

c. List the most likely genotypes with respect to the albino trait for the eight people shown in this pedigree.

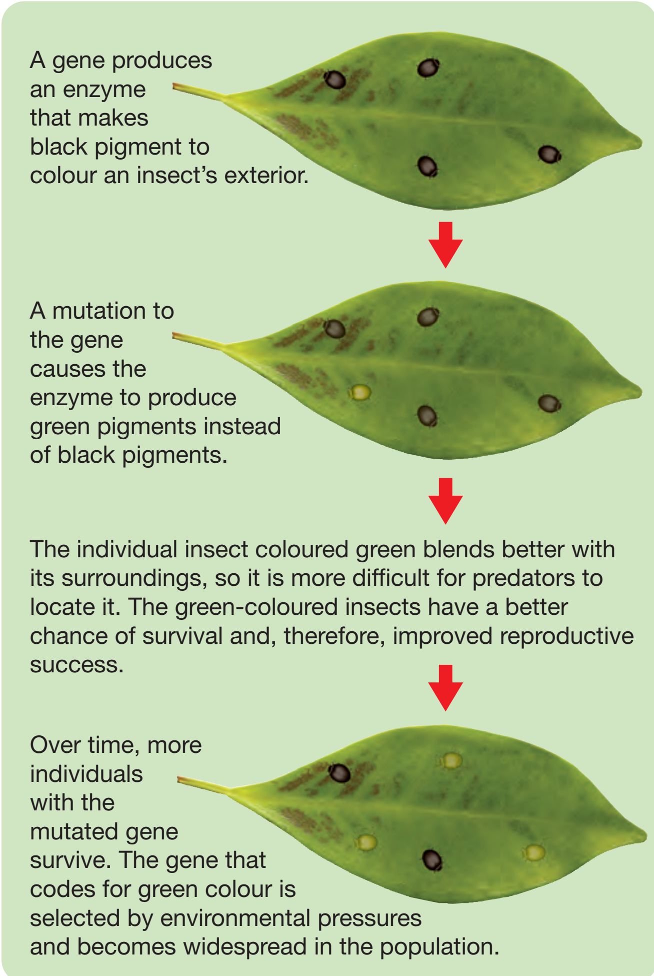
43. Sonja is not able to roll her tongue but her brother, Mikail, can roll his tongue. When Sonja surveys her family members, she finds that her mother is a tongue roller, and her father is not. Her father's only sister and brother cannot roll their tongues either. The two grandparents on Sonja's father's side are also non-tongue rollers. For the grandparents on the mother's side, the grandfather is a tongue roller, but the grandmother is not. Develop a pedigree for the family described.

44. Phenylketonuria (PKU) is a genetic disease caused by an inability to produce an enzyme. This missing enzyme causes a buildup of an amino acid in the body to toxic levels—this can result in organ damage and impaired intellectual development. Draw a pedigree for the following description of a family's genetic history for the autosomal recessive disease of phenylketonuria.

A male who does not exhibit PKU and a female who does not exhibit PKU have four boys. The two oldest sons are carriers of the recessive allele, and the youngest son develops the genetic disease. The third son neither has the disease nor is he a carrier. The oldest son has two daughters with another PKU carrier—both of these daughters develop the PKU genetic disease.

Beneficial Mutations Affect Populations—Evolution

You have learned that most mutations have little effect on an organism's functioning. In rare cases a mutation can impair a gene's ability to produce a protein, and this results in the disease symptoms. A mutation occasionally creates an advantage for the individual.



Perhaps the mutation causes a brighter colour of flower to be produced, which makes the flower with the mutation more successful at attracting pollinators.

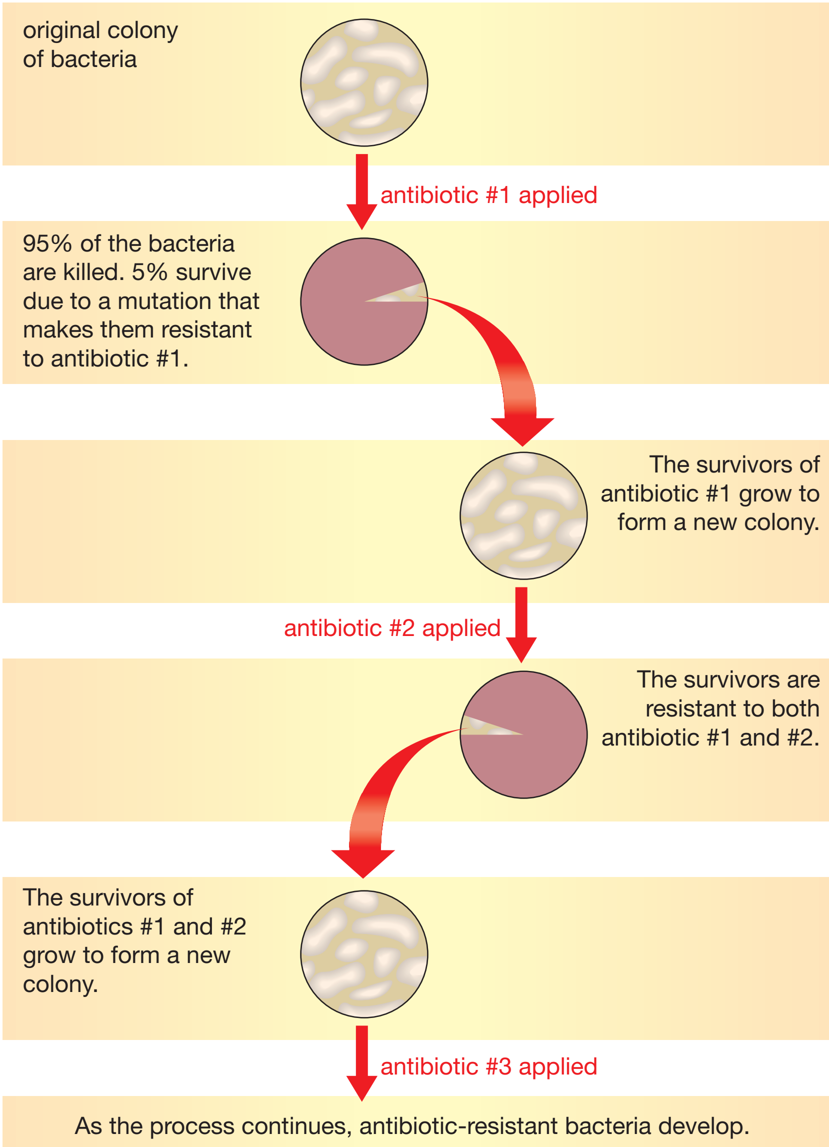
Or perhaps a mutation in genes controlling its colour provides the individual with improved camouflage to help protect it from predators.

In cases where mutations result in an advantage to the organism's survival, organisms possessing the mutation have a better chance to survive and breed. This means that this new variety is able to generate a greater number of offspring.

Perhaps you may recall from previous science courses that Charles Darwin used the term "survival of the fittest." This refers to the idea that the organisms best able to survive have the opportunity to reproduce and pass along their traits to their offspring. Mutations play a key role in this process of natural selection because they introduce the new alleles selected by the environment as being more favourable. In this way, advantageous traits become more widespread in a population and change a population's overall characteristics.

Resistance in Bacteria

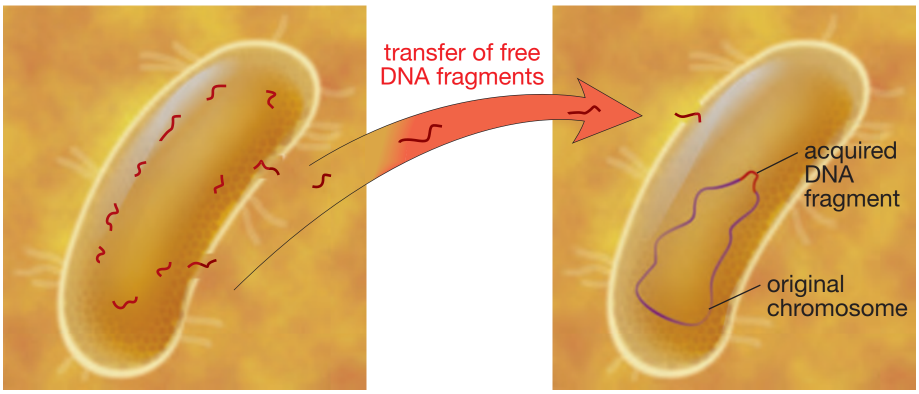
Antibiotics are chemicals that have saved countless lives by killling bacteria that cause infections and illnesses. When antibiotics are used, most of the bacteria die. Recently, the number of infectious bacteria resistant to antibiotics has increased. You have seen how mutations can result in the change or evolution in a species. Can mutations in bacteria be the cause of an increase in resistance to antibiotics?



If some bacteria possess a mutant gene that makes them resistant to antibiotics, they will not be killed. The resistant bacteria not killed by the antibiotic are the only individuals remaining to reproduce. Over time the new population—or strain—of bacteria consists almost entirely of members that possess genes resistant to that antibiotic. Each time a bacterial population is exposed to a new antibiotic, this process of natural selection repeats and only the resistant survive. Many scientists and doctors are becoming worried about the development of bacterial strains that are resistant to antibiotics. For this reason, antibiotics are prescribed less frequently than before, and patients who are prescribed antibiotics are advised to take all their medication even after they have begun to feel better to make certain a large percentage of the bacterial population is killed.

The process of antibiotic products "selecting" resistant bacteria is based not only upon the same principles of selective breeding that you studied earlier in this chapter, but upon the same principles of natural selection that you examined in earlier science courses. The main idea here is that individuals most suitable to a particular environment live to breed and pass on their genes.

Transformation of DNA Fragments

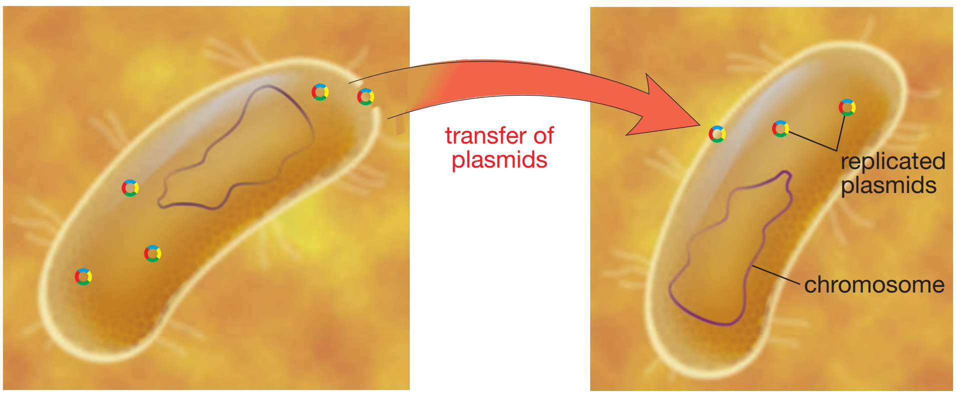


a dead bacterium

a living bacterium acquiring DNA from environment

As you learned earlier, evolution takes place over long periods of time and involves many generations. Because bacteria reproduce very quickly—as fast as once every 20 minutes—the speed of their evolution can appear to be rapid. The appearance of bacterial superbugs resistant to several kinds of antibiotics has made the scientific community question the exact mechanism for the evolution of this trait. Even though bacteria reproduce asexually, they have methods of exchanging DNA that create more genetic diversity and can result in the development of new traits, such as antibiotic resistance. Some bacteria can acquire foreign DNA from their surrounding environment and incorporate it into their own DNA in a process known as **transformation**.

Transformation of Plasmids



a living bacterium with plasmids

a bacterium acquiring plasmids

Many bacteria can also possess a small circular piece of DNA molecule, called a **plasmid**, which is separate from the DNA in the bacteria's chromosome. Plasmids are self-replicating and some have the ability to temporarily join to the bacterial DNA. The plasmids may only have a few genes not necessary for the regular functioning or survival of the bacteria, but these genes may influence other traits or lead to advantageous properties for the organism—this may include antibiotic resistance. Bacteria with a plasmid containing genes that provide antibiotic resistance make the bacteria exposed to antibiotics resistant to the drugs. Because plasmids can be transferred quite easily between bacterial cells when they contact one another, a plasmid can be transferred between individuals. This results in the sharing of antibiotic-resistant genes.

transformation: the process by which free DNA is incorporated into a bacterial cell

plasmid: a self-replicating circular piece of DNA that can be transferred between bacteria

Plasmid transfer allows for the sharing of genes on the plasmids between bacteria.

2.4 Summary

Mutations are changes in the sequence of DNA that can be inherited by future generations. These changes spontaneously occur and do not usually affect an individual. Mutations occasionally impair gene functioning or result in beneficial advantages. They can occur when nucleotides are substituted by point mutation, while deletions or additions of nucleotides result in frameshift mutation. Mutations that improve an organism's success within a population lead to adaptations selected by the environment. Natural selection is what drives the process of evolution. Resistance to antibiotic drugs has occurred in bacteria as a result of mutation, transformation, plasmid transfer, and natural selection.

A genetic disease is an illness resulting from faulty or impaired genes that can be inherited by future generations. The presence of two alleles for each gene in the human genetic make-up helps prevent the development of many genetic diseases. Individuals can be carriers of alleles that cause genetic diseases.

The pattern of inheritance for genetic diseases is the same studied previously for autosomal, sex-linked, dominant, or recessive alleles. Punnett squares can be used to predict the probability of offspring inheriting a genetic disease when the disease is caused by a single gene. Pedigrees can be used to trace the inheritance of a genetic disease in a family.

2.4 Questions

Knowledge

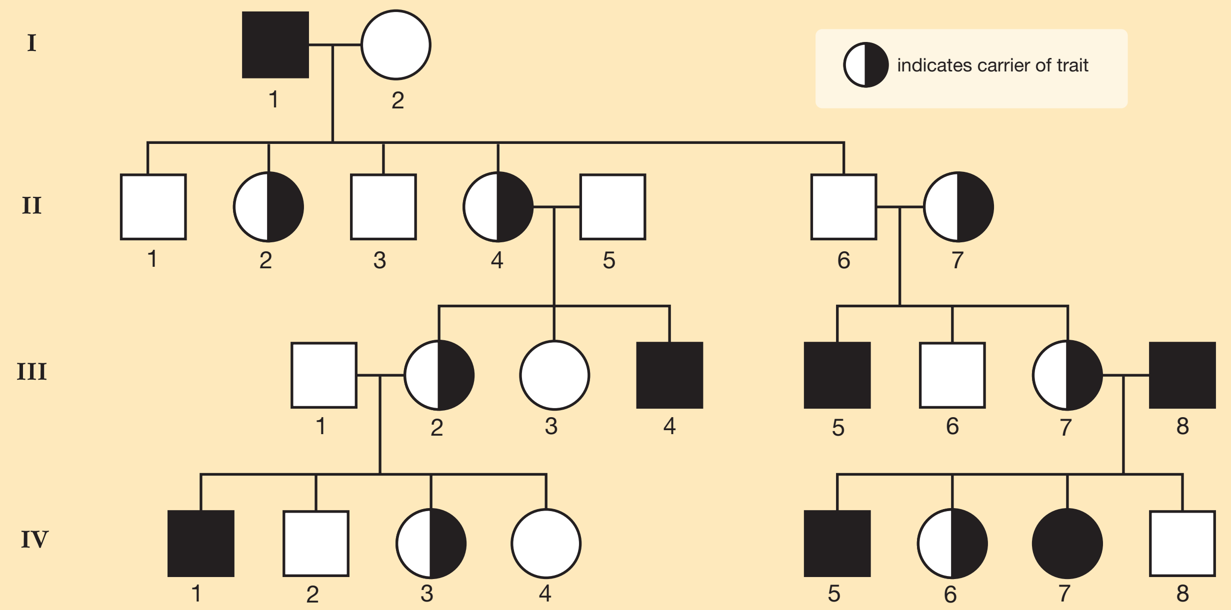
1. Define *mutation*.

2. Explain why a doctor may ask questions about the history of certain traits or illnesses in your family.

3. Explain how people who are carriers of the allele for cystic fibrosis do not have disease symptoms.

4. Red-green colour-blindness is a sex-linked trait. The pedigree in "Inheritance of Red-Green Colour-Blindness" shows the occurrence of the colour-blindness disorder for one family. Study the diagram and answer the following questions.

Inheritance of Red-Green Colour-Blindness



a. In the first generation, is the father or the mother colour-blind?

b. Determine the number of males and the number of females produced by the father and mother of the first generation.

c. State the number of individuals in this pedigree who are carriers for colour-blindness.

d. How many males and how many females have colour-blindness in this pedigree?

5. List several mutagens that can increase the frequency of mutations.

Applying Concepts

6. List two similarities and two differences between Punnett squares and pedigree charts.
7. Despite new therapies and other medical breakthroughs, cystic fibrosis and other genetic diseases can still cause death before adulthood. Identify the significance of the symptoms of Huntington disease not usually appearing until later in a person's life.
8. Explain why your reproductive organs are usually shielded with lead sheets during an X-ray.

Use the following information to answer question 9.

Sickle cell anemia is an autosomal recessive genetic disease. The impaired gene causes red blood cells to be produced that are shrunken sickle shapes rather than the normal round disc shapes. These deformed red blood cells can block narrow blood vessels. People with two recessive sickle cell alleles become very ill and often die while they are very young. Most people who suffer from sickle cell anemia or carry the recessive gene tend to be from areas affected by malaria, which is a deadly disease carried by mosquitoes. The malaria parasite reproduces inside a person's red blood cells. People who are carriers of one of the mutated sickle cell anemia alleles actually have an advantage over non-carriers—they are resistant to malaria. This accounts for the fact that this allele is more common in people from areas affected by malaria.

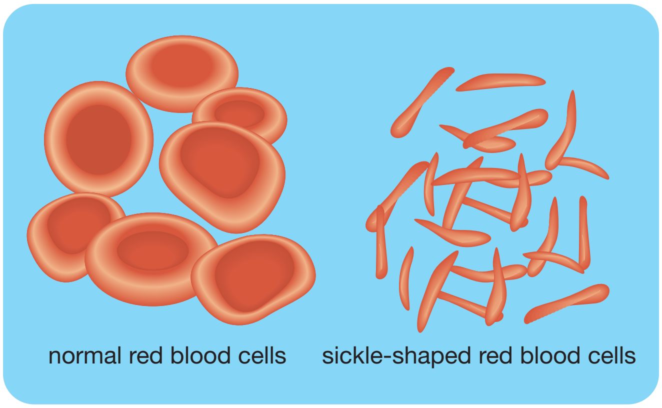


Figure A2.19: The distribution of malaria prior to mosquito control programs is highlighted on this map by green shading.

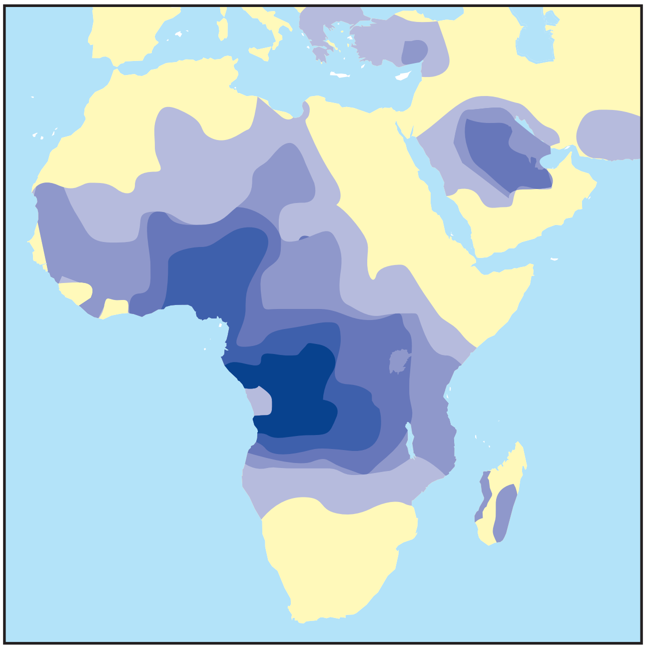
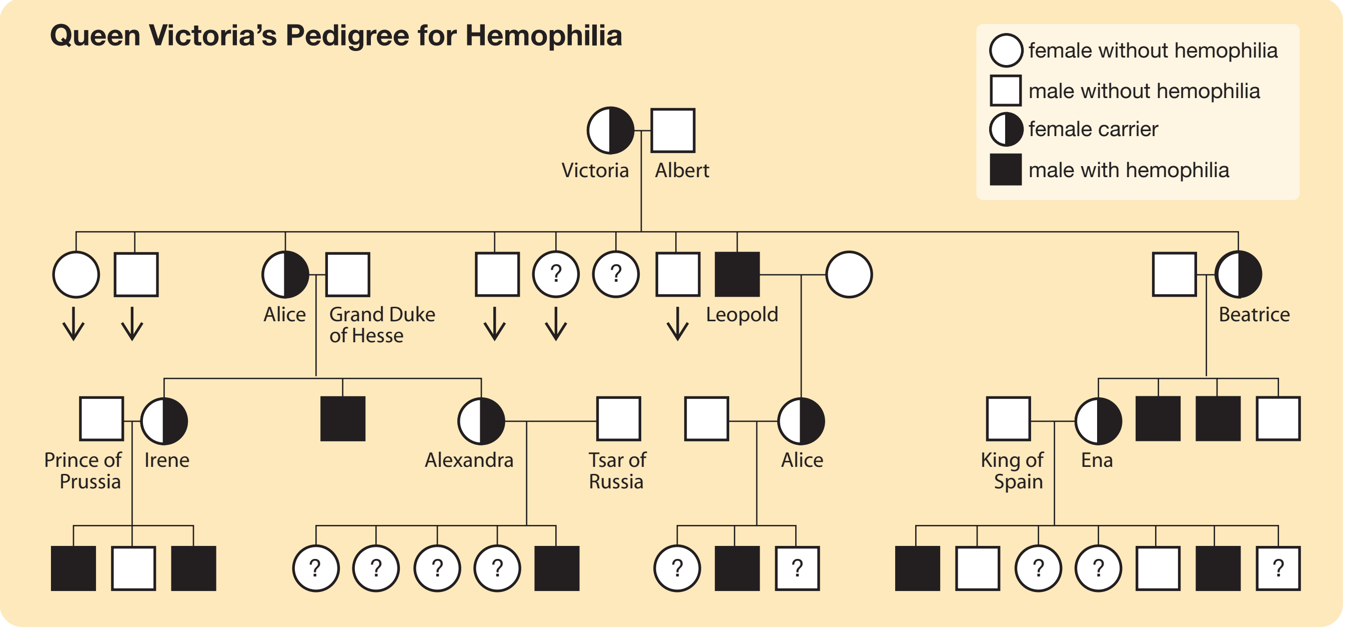


Figure A2.20: This map shows the distribution of sickle cell disease. The darker the shade of purple, the greater the percentage of people who have the disease.

9. **a.** Use a Punnett square to show the probable results of the cross between two people who are heterozygous for the sickle cell trait (*Ss* × *Ss*) and are malaria resistant.
   b. List the possible genotypes of the children from this couple.
   c. State the probability of a child of this couple being resistant to malaria.
   d. State the probability of a child of this couple developing sickle cell anemia.
   e. Explain why the sickle cell anemia allele is more common in areas infected with malaria.

Use the following information to answer question 10.

Queen Victoria of England was a carrier of the sex-linked genetic disease called hemophilia. Victoria had many children, but only one of them developed hemophilia. Several of her children married into other European royal families and passed on Victoria's hemophilia allele. The most famous case of hemophilia was Victoria's great-grandson Alexei, the heir to the Russian throne. The controversial historical figure Rasputin gained influence with the Russian royal family by claiming to be able to heal Alexis' hemophilia.



10. Study the pedigree of Queen Victoria's descendants. Then answer questions 10.a. to 10.c.

a. The royal family's ancestry is well documented. There is no history of hemophilia in any of Queen Victoria's ancestors. Explain how you think the hemophilia defect appeared in her genes.

b. Explain why the individuals with hemophilia in this pedigree are all males.

c. Why are question marks written on some of Queen Victoria's female descendants?